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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,178	09/09/2003	David Jonathan Madge	2451.0090006	7469

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WASHINGTON, DC 20005

EXAMINER

VALENROD, YEVGENY

ART UNIT	PAPER NUMBER
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1621

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/659,178

Applicant(s)

MADGE ET AL.

Examiner

Yevgeny Valenrod

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 24,25 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23,26-28 and 30-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 9/09/2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :1/26/06; 9/19/05;
5/27/05; 10/20/04; 9/17/04; 8/23/04; 3/19/04; 2/24/04.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-23, 26-28 and newly added claims 30-38, in the reply filed on 5/12/06 is acknowledged. The traversal is on the ground(s) that searching all of the inventions together does not present a serious burden. This is not found persuasive because the groups are directed to different classes of invention, a method of use, a compound and a method of making the compound. References teaching a method of making the compound will not necessarily teach a method of using the said compound. In the event that the compound is found allowable applicant is entitled to rejoinder of the method claims as was indicated in the office action sent on 4/10/06, in which case groups II and III will be examined.

Claims 24, 25 and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/12/06.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 recites the limitation "consists essentially of an acid salt" in the first line of the claim. There is insufficient antecedent basis for this limitation in the claim. The independent claim one is directed to base addition salts not acid salts.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-18, 21, 22, 23, 26-28 and 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rewinkel et al. (Current Pharmaceutical Design, 1999, 5, 1043-1075) in view of de Nanteuil et al. (US 5,814,622) and in further view of Adams et al. (US 5,780,454).

Instant claims 1-18, 21, 22, 23, 26-28 and 30-36 are directed to a pharmaceutically acceptable base addition salt of a boronic acid of formula (I) in claim 1, or formula (II) in claim 14 and to formulation of the said salt in claims 26-28.

Scope of prior art

Rewinkel et al. teach a compound of formula 21 (page 1052, bottom left of Table 3). The said compound is a boronic acid that has the methoxyalkyl substituent for R⁹ in the instant claim 1, a Pro amino acid residue, which satisfies the structural limitation of claim 17, a hydrophobic moiety presented by the diphenylalanine residue, and a protected N-terminal amine group. Renkwel et al. Provide K_i for thrombin inhibition in

the table on the bottom of page 1052. Compound 21, has K_i of 14 nM, which is below 100nM as claimed in claims 7 and 28.

Ascertaining the difference between prior art and the instant claims

Rewinkel et al. teach the organic component of the instantly claimed organoboronic acid salt. They also teach the boronic acid attached to the organic component in a position consistent with the structural limitations of the instant claims. However, they fail to teach the pharmaceutically acceptable salt of the boronic acid.

Secondary reference

Nanteuil et al. Describe compound of formula (I/g) (organoboronic acid) and pharmaceutically acceptable salts thereof (column 6, lines 20-36). The pharmaceutically acceptable salts include both base and acid addition salts. In Column 3, lines 32-34 Nanteuil et al. describe examples of counterions for base addition salts. Said examples include Sodium, Potassium and amines.

Motivation and obviousness

It is obvious to form salts from known acids. In re Williams, 89 USPQ 396 (CCPA 1951). Rewinkel et al. teach compound 21, which is the acid of the instantly claimed pharmaceutically acceptable salt. At the time the instant invention was made, one of ordinary skill in the art looking to alter the permeability, solubility, or other physiological properties commonly associated with producing pharmaceutically acceptable salts of known acid (see Davies et al, The pharmaceutical journal, 2001, Vol 266, p 322-323; particularly page 322, column 1, first paragraph) would have been motivated to prepare a salt of the organoboronic acid 21 described by Rewinkel et al.

Art Unit: 1621

Such a modification would not be new to the art. Nanteuil et al describe pharmaceutically acceptable salts of organoboronic acids and thus provide an expectation of success for performing the said modification. Nanteuil et al. do not limit themselves to the counterion examples that are listed in column 3 lines 32-34. They specifically mention that these examples are provided without any limitation. One of ordinary skill in the art would be motivated to produce various pharmaceutically acceptable salts in order to achieve the desired properties of the pharmaceutical agent. Pharmaceutically acceptable salts of organoboronic acids salts include alkaline metal salts, alkaline earth metal salts (including calcium) and amine salts (Adams et al. US 5,780,454; column 9, lines 57-65). In the absence of some unexpected properties for the base addition salts of organoboronic acids of the instantly claimed compounds, the invention is seen to be prima facie obvious in view of the prior art of record and the case law cited herein.

Double Patenting

Claims 1-23, 26-28 and 30-38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 23 and 25 of U.S. Patent No. 7,122,572 ('572). Although the conflicting claims are not identical, they are not patentably distinct from each other because the all the limitations of the instant claims are found in the sited claims of ('572).

Instant claims are directed to a pharmaceutically acceptable base addition salt of a boronic acid of formula (I) in claim 1, or formula (II) in claim 14 and to formulation of the said salt in claims 26-28.

Claim 2 of '572 claims a structure that encompasses the structure of the instant claim 1. Claim 12 of '572 displays a structure that is identical compound of formula (II) in the instant claim 14. Claims of '572 that directed to a salt and are dependent on claims 2 and 12 have all of the limitations of the instant claims 1-23 and 30-38. The formulations and medicament claimed in the instant claims 26-28 are obvious over claims 20, 23 and 25 of '572. The said formulation and medicament claims differ from the instant invention in that the compounds from which the formulation and medicament is made are not identical to the compound in '572. However, compound (III) of '572 encompasses all of the instantly claimed compounds, and compound (IV) of '572 is specie of the instantly claimed compound (I).

In looking in continuity data, it is noted that the applicant has several pending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar and submit the appropriate Terminal Disclaimer(s). See copending applications # 10/937,854 and 11/078,097

Conclusion

Claims 1-38 are pending.

Claims 24, 25 and 29 are withdrawn as pertaining to non-elected subject matter.

Art Unit: 1621

Claims 1-23, 26-28 and 30-38 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yevgeny Valenrod whose telephone number is 571-272-9049. The examiner can normally be reached on 8:30am-5:00pm M-F.

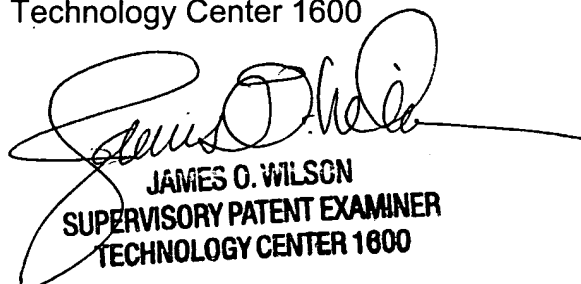
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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